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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/005,133	12/05/2001	Mark Ledeboer	VPI/00-126 US	8058

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EXAMINER	
TRUONG, TAMTHOM NGO	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 04/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/005,133	LEDEBOER ET AL.	
	Examiner	Art Unit	
	Tamthom N. Truong	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 9-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 9-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 2.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL ACTION

Applicant's amendment of 12-23-03 has been fully considered. It is appreciated that the amendment has deleted non-elected subject matter. While the amended specification has clarified the definition of "aliphatic group", the amended claims 2-5 have not overcome the rejection of 112/2nd for "lack antecedent basis", thus said rejection is maintained for claims 2-5. Also, it is noted that the proviso in claim 1 does not have support in the specification, and thus, constitutes new matter. Furthermore, the amended method claims, and new method claims raise a new ground of rejection.

Claim 8 is cancelled, therefore, only claims 1-7, and 9-19 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 2-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

   a. Claims 2 and 3 lack antecedent basis because they recite the limitations of "*CH_2substituted heterocyclyl*" and "*substituted heterocyclyl*" which are not recited **in** the definition of R^2 and R^3 **in** claim 1. Another words, claim 1 does not allow for an *optionally substituted* heterocyclyl group, and thus, does not provide antecedent basis for

a *substituted* heterocyclyl. The limitations of claims 2 and 3 must have antecedent basis from the claim they depend on, which is claim 1, and not from the specification.

b. Despite the amended claim 3 which includes the limitation of "-CH_2(aryl)", claims 4 and 5 still lack antecedent basis because the limitation of "*benzyloxymethyl*" (or, benzyl-O-methyl) does not fall within the group "CH_2(aryl)", nor does it fall within the group "-CH_2OR".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. **New Matter:** Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The added proviso in claim 1 does not have support in the specification, and thus, constitutes new matter. It is recognized that applicants intend to overcome the teaching of WO 00/31063. However, **Even a negative limitation requires description, *Ex Parte Grasselli*, 231 USPQ 393.**

Claims 2-6, 17, 20, and 21 are also rejected under 35 U.S.C. 112, first paragraph for being dependent on claim 1, and carry over the proviso with no support in the specification.

3. **Enablement:** Claims 7, 9-16, 18, and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The scope of the claims: Claims 7-16 call for a method of treating virtually every disease known in the art. Furthermore, the method of treating some diseases seems contraindicated in others. For example, the treatment of "*proliferative disorders*", which requires the inhibition of cell growth (of all cell types), would be contraindicated in the treatment of "*neurodegenerative diseases*", which requires the inhibition of cell death (particularly, inhibiting neuron death). Likewise, the treatment of "*autoimmune diseases*", which requires the suppression of the immune system, would be contraindicated in the treatment of "*infectious diseases*", which requires the activation of the immune system. Furthermore, many of the listed diseases do not have a known etiology. For example, multiple sclerosis, psoriasis, Huntington's disease, Crohn's disease, etc. have never had a known cause. Also, the cited diseases affect different organs, or tissues, and have an entirely different pathophysiology. For instance, rheumatoid arthritis and osteoporosis affect the joints and bones in very different ways.

That is, osteoporosis is asymptomatic while rheumatoid arthritis is associated with pain and stiffness in the joints. Similarly, Grave's disease affects the thyroid while Crohn's disease affects the gastrointestinal system. Thus, the claimed method treats the body virtually from head to toes, and inside out.

Claims 18 and 19 recite a "method of inhibiting JNK activity" which is not directed to a particular disease, and encompass a method of treating any of the diseases in claims 7-16, which are too diverse to warrant predictability.

The guidance provided: The specification only provides *in-vitro* results for a few compounds, and does not provide an *in-vivo* assay. Thus, even for the inhibition of JNK activity, it is not sufficient to conclude that all compounds of the claimed genus could inhibit JNK. Thus, the provided guidance is not adequate to allow a skilled clinician to apply any of the claimed compounds to the treatment of any disease.

The state of the art: There is nothing in the art that relates analogous compounds to the inhibition of JNK, and/or the treatment of any of the recited diseases.

Thus, with the unpredictable nature of the art, and limited guidance, the skilled clinician would have to carry out undue experimentation to practice the claimed method with compounds of formula I.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Utility: Claims 18 and 19 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either an asserted utility or a well established utility. A revised utility guideline requires that utilities must be specific, substantial, and credible. By specific, said guideline calls for a particular disorder or disease. In the case of cancer treatment, a specific type of cancer must be indicated. By substantial, said guideline requires that utilities must define a "real world" use, and must not constitute further research to identify or reasonably confirm a "real world" context of use. In the instant case, said claims call for a "*method of inhibiting JNK activity*", which is not specific and not substantial as the specification does not appear to relate a specific disorder to said method. Furthermore, said method is not a well known method, and thus requires extensive further research.

Note, the specification relates the inhibition of JNK to a myriad of diseases such as: inflammatory diseases, autoimmune diseases, destructive bone disorders, proliferative disorders, cancer, infectious diseases, neurodegenerative diseases, allergies, reperfusion/ischemia in stroke, heart attacks, angiogenic disorders, organ hypoxia, vascular hyperplasia, cardiac hypertrophy, etc. None of those diseases shares the same etiology, nor do they affect the same organ or tissue. Such a diverse group of diseases does not satisfy the first requirement of the utility guideline, which is specificity. Athough claim 19 is applicable to a "*biological sample*", it still does not have a specific use because the phrase "*biological sample*" includes petri-dish specimens, and animal models. Thus, the method recited in claims 18 and 19 do not have an asserted utility.

Because applicant has not disclosed any specific and substantial utility for the claimed invention, credibility will not be assessed. See Brenner v. Manson, 148 USPQ 689, and In re Zeigler, 26 USPQ 2d 1600, 1603 (Fed. Cir. 1996).

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M-F (~10 am ~ 6:30 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached at 571-272-0674. If you are unable to reach Dr. Shah within a 24 hour period, please contact James O. Wilson, Acting SPE of 1624, at 571-272-0661.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

T. Truong
April 16, 2004

RICHARD L. RAYMOND
PRIMARY EXAMINER
ART UNIT 1624